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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/616,210	07/08/2003	Michael S. Kopreski	00-1313-D	9776

7590 03/21/2007

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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/616,210	KOPRESKI ET AL.	
	Examiner	Art Unit	
	Frank W. Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *1-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on January 3, 2007 has been entered. The claims pending in this application are claims 1-36 wherein claims 1-20 have been withdrawn due to restriction requirement. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on January 3, 2007.

Election/Restrictions

2. This application contains claims 1-20 drawn to an invention nonelected with traverse in the response filed on October 21, 2005 and January 11, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

3. Claim 21 is objected to because of the following informality: "trophoblast tissue" in last line of the claim should be "the trophoblast tissue" in order to correspond to "trophoblast tissue" in preamble.

4. Claim 26 or 29 is objected to because of the following informality: "A method" should be "The method".

5. Claim 21 is objected to because of the following informality: "a woman post-partum" should be "a post-partum woman"

Appropriate correction is required. Note that applicant does not address this issue.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Enablement

Claims 21-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The claims are drawn to a method of detecting, monitoring or evaluating trophoblast tissue in a pregnant woman, a woman post-partum or woman with an antecedent pregnancy by detecting 5T4 RNA in serum or plasma of a pregnant woman, a post-partum woman or woman with an antecedent pregnancy, a method of monitoring a placenta during a pregnancy by detecting 5T4 RNA in a bodily fluid or serum from a pregnant woman, a method of detecting 5T4 RNA in a bodily fluid from a pregnant or post-partum woman for detecting, diagnosing,

monitoring or evaluating a placenta disease or condition by detecting 5T4 RNA in a bodily fluid of a pregnant woman or a post-partum woman, and a method of detecting trophoblast RNA in a blood plasma or serum from a woman for detecting, diagnosing, monitoring or evaluating a placental tissue by detecting 5T4 RNA in serum or plasma from a woman. The invention is an class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." *Mycogen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The Breadth of The Claims

Claims 21-23 and 26 encompass a method of detecting, monitoring or evaluating trophoblast tissue in a pregnant woman, a woman post-partum or woman with an antecedent pregnancy by detecting 5T4 RNA in serum or plasma of a pregnant woman, a post-partum woman or woman with an antecedent pregnancy. Claims 24, 25, and 27-29 encompass a method of monitoring the placenta during pregnant by detecting 5T4 RNA in any kind of bodily fluid or serum of a pregnant woman. Claims 30-33 encompass a method of detecting 5T4 RNA in any kind of bodily fluid from a pregnant or post-partum woman for detecting, diagnosing, monitoring or evaluating a placenta disease or condition by detecting 5T4 RNA in any kind of bodily fluid of a pregnant woman or a post-partum woman. Claims 34-36 encompass a method of detecting trophoblast RNA in a blood plasma or serum from a woman for detecting, diagnosing, monitoring or evaluating a placental tissue by detecting 5T4 RNA in serum or plasma from a woman.

Working Examples

The specification provides working examples (see pages 14-16) for detecting 5T4 mRNA in normal human placenta and lung and breast from lung and breast cancer patients and detecting 5T4 mRNA from serum from lung and breast cancer patients. The specification provides no working example for detectiing 5T4 RNA in any kind of bodily fluid or serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy.

The Amount of Direction or Guidance Provided and The State of The Prior Art

Although the specification teaches to detect 5T4 mRNA from serum of certain cancer patients such as breast and lung cancer patients (see the specification, pages 14-16), the specification does not provide a guidance to show detection of 5T4 RNA in any kind of bodily fluid or serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy so that trophoblast tissue and placenta disease or condition can be detected, diagnosing, monitored or evaluated as recited in claims 21-36. Furthermore, there is no experimental condition and/or experimental data in the specification to support the claimed invention. Although it is known in the art that human trophoblast tissue and placenta express high level of 5T4 (see table 1 in Southall et al., Br. J. Cancer, 61, 89-95, 1996), during the process of the prior art search, the examiner has not found any prior art which is related to detect 5T4 RNA in any kind of bodily fluid or serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy so that trophoblast tissue and placenta disease or condition can be detected, diagnosing, monitored or evaluated as recited in claims 21-36.

Level of Skill in The Art, The Unpredictability of The Art, and The Quantity of Experimentation Necessary

While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether 5T4 RNA can be detected in any kind of bodily fluid or serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy so that trophoblast tissue and placenta disease or condition can be detected, monitored or evaluated as recited in claims 21-36. Although it is known in the art that human trophoblast tissue and placenta express high level of 5T4 (see table 1 in Southall et al., Br. J. Cancer, 61, 89-95, 1996), there is no evidence to show that 5T4 RNA can be detected in any kind of bodily fluid such as urine or serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy. Furthermore, even we assume that 5T4 RNA can be detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy, there is no evidence to show that 5T4 RNA detected in serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy must come from human trophoblast tissue or placenta so that trophoblast tissue or placenta disease or condition can be detected, monitored or evaluated as recited in claims 21-36. With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether 5T4 RNA can be detected in any kind of bodily fluid or serum or plasma from a pregnant woman, a post-partum woman or woman with an antecedent pregnancy.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high, the specification provides one with no guidance that leads one to claimed methods. One of skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples and the no teaching in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Response to Arguments

In page 14, last paragraph of applicant's remarks, applicant argues that "[A]pplicants respectfully contend that their specification fulfills the enablement requirement of 35 U.S.C. §112, first paragraph throughout the scope of the pending claims, and request that the Examiner withdraw this ground of rejection".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because applicant does not provide evidence to show how their specification fulfills the enablement requirement of 35 U.S.C. §112, first paragraph throughout the scope of the pending claims.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 22, 23, 26-28, 31, 32, and 34-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 21 is rejected as vague and indefinite. Since step a) only states that "extracting RNA from blood plasma or serum", it is unclear that RNA from blood plasma or serum in step a) of the claim is from a pregnant woman, a post-partum woman or a woman with an antecedent pregnancy or not. Please clarify. Note that applicant does not address this issue.

11. Claims 22, 27, 31, and 35 are rejected as vague and indefinite because amplifiable RNA reporters are not an amplification reaction but are products. Please clarify.

Response to Arguments

In page 14, second paragraph of applicant's remarks, applicant argues that "[A]pplicants note that these species were explicitly disclosed throughout their specification. Also, the skilled worker would recognize that these species partake in linear amplification reactions used routinely to quantify nucleic acid amounts; see, for example, Lau et al., 'Linear amplification of catalyzed reporter deposition technology on nylon membrane microarray,'Centre National de la Recherche Scientifique, at http://cat.inist.fr/?aModele=afficheN&cpsidt=13904712). Applicants thus respectfully contend that the skilled worker would understand the uses of these species in their claimed invention, and request that this ground of rejection be withdrawn".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because amplifiable RNA reporters are not an amplification reaction but are products and the reference from Lau *et al.,* did not indicate that amplifiable RNA reporter is a method as argued by applicant.

12. Claims 23, 28, 32, and 36 are rejected as vague and indefinite. Since ELISA detection is enzyme-linked immunosorbant assay, it is unclear how ELISA detection can include methods using biotinylated or otherwise modified primers, laser-induced fluorescence, Southern blot analysis, Northern blot analysis, reverse dot blot detection, or high-performance liquid chromatography. Please clarify.

Response to Arguments

In page 14, third paragraph of applicant's remarks, applicant argues that "[A]pplicants point out that the skilled worker would recognize that the limitation is properly understood to be read 'ELISA detection using biotinylated or modified primers.' Thus, in non-limiting example, an antibody specific for a reporter (such as biotin or other molecule) can be used to detect the specific presence of a particular nucleic acid species. Applicants thus respectfully contend that the skilled worker would understand the uses of these species in their claimed invention, and request that this ground o f rejection be withdrawn".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because the phrase "ELISA detection, including methods using biotinylated or otherwise modified primers, labeled fluorescent or chromogenic probes, laser-induced fluorescence, Southern blot analysis, Northern blot analysis, electrochemiluminescence, reverse dot blot detection, or high-performance liquid chromatography" recited in claims 23, 28, 32, and 36 is read as that ELISA detection includes methods using biotinylated or otherwise modified primers, labeled fluorescent or chromogenic probes, laser-induced fluorescence, Southern blot analysis, Northern blot analysis, electrochemiluminescence, reverse dot blot detection, or high-performance liquid chromatography" and ELISA detection using biotinylated

or modified primers argued by applicant can be read as Southern blot analysis, Northern blot analysis and reverse dot blot detection, or high-performance liquid chromatography.

13. Claim 29 recites the limitation "the gestational trophoblastic disease" in the claim. There is insufficient antecedent basis for this limitation in the claim since there is no "gestational trophoblastic disease" in claim 24. Please clarify.

14. Claim 34 is rejected as vague and indefinite in view of the phrase "wherein placental tissue is detected, diagnosed, monitored or evaluated" because the phrase "placental tissue is diagnosed" does not make sense. Please clarify.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 24-36 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 24-36 and 39-41 of copending Application No.10/363,023. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). Although claims 24-36 in this instant application are not identical to claims 24-36 and 39-41 of copending Application No. 10/363,023, claims 24-36 and 39-41 in copending Application No. 10/363,023 are directed to the same subject matter and fall entirely within the scope of claims 24-36 in this instant application. In other words, claims 24-36 in this instant application is anticipated by claims 24-36 and 39-41 of copending Application No. 10/363,023.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

In page 15, first and second paragraphs of applicant's remarks, applicant argues that "[A]pplicants acknowledge this rejection and will address this ground of rejection by filing a Terminal Disclaimer when the Examiner indicates that the claims are otherwise in condition for allowance".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because applicant does not file a terminal disclaimer.

Conclusion

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. No claim is allowed.

19. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of

such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is (571)273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571)272-0735.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

March 12, 2007

FRANK LU
PRIMARY EXAMINER